CONFOUNDING FACTORS

Introduction

According to a 1990 publication by a Swedish scientist, Dr. Ragnar Rylander:

> Studies evaluating the hypothesis of a relationship between exposure to environmental tobacco smoke and lung cancer must take into account other environmental risk or protection factors and the possibility that exposure to environmental tobacco smoke may be confounded. This has not been done in the majority of such studies. Until this has been done, the claim of causality between environmental tobacco smoke and lung cancer remains uncertain. [Emphasis added.][1]

In epidemiologic studies, confounders are variables which can affect the outcome of interest, independently of the factor under investigation. Potential confounding factors in studies of ETS and lung cancer are numerous and varied.[2] It is difficult to control for all of them in the design of an epidemiologic study. Following are lists of some of the possible confounders encountered in epidemiologic studies of lung cancer incidence in nonsmokers, both those specifically considering ETS and those dealing with other factors.

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Heating and Cooking Fuels

- In developing countries, the use of certain fuels (kerosene, gas, coal, liquefied petroleum gas, straw, or wood) for heating and cooking contributes to elevated levels of indoor air pollution, which may contribute to disease incidence.[3]

- Following earlier, limited reports[4] on exposures to fumes from the use of various fuels, eight studies examining coal use in stoves and other indigenous heating devices in China have recently been published.[5-12] RRs as high as 14 have been reported,[8] although most RRs are in the 1.0 to 2.0 range.[11,12]

- Some fuels, namely, kerosene or coal and wood or straw, have been associated with a increased risk of lung cancer in Japanese women as well.[13,14]

Cooking Techniques

- The use of certain cooking oils and some cooking techniques (i.e, stir-frying and deep frying) which produce oil vapors have been associated with increased lung cancer risks in Chinese women.[11,15]

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Air Pollution

- In addition to indoor air pollution from heating and cooking fuels, as described above, outdoor air pollution has been associated with increased lung cancer incidence in at least one epidemiologic study in northeast China.[12]

Dietary Factors

- Increased lung cancer risk has been associated with the consumption of smoked, salted, cured, pickled, processed, or spicy foods among Oriental women.[18] Additionally, research suggests that wives whose husbands smoke may consume more processed and spicy foods and eat fewer fresh fruits and vegetables than do those whose husbands do not smoke.

- One study reported an elevated lung cancer risk among Oriental women associated with the consumption of green or black tea.[17]

- It has also been reported that nonsmokers married to smokers have lower intakes of dietary carotene, a substance associated with decreased cancer risks when consumed in sufficient amounts.[18] Recently, an abstract reported an correlation between serum carotene levels and socioeconomic status; this

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could be important if smoking and SES are also correlated, as has been suggested.

Occupation

- Some of the studies considering lung cancer in nonsmokers have also reported elevated relative risks associated with employment in certain fields or with occupational exposures to certain substances.[5,11-13]

Medical and Lifestyle Factors

- Personal health factors such as menstrual cycle length and previous history of respiratory disease (including tuberculosis, pneumonia or emphysema) have been associated with increased risk for lung cancer.[5,9,11,15]

- Family history of lung cancer has also been associated with increased lung cancer risk.[9,11]

- An association between husband's smoking status and family lifestyle has been reported.[16] Wives with husbands who were nonsmokers had better SES, were more conscientious housewives, ate better diets, had higher indices of family cohesiveness,

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and had better indices of overall health than did women married to smokers.

- At least one hobby, keeping pet birds, has been associated with increased lung cancer risk.[19]

Conclusion

While of general importance, the question of confounders appears to be particularly relevant in studies of Asian women. Certain cultural variables (e.g., use of smoky fuels, certain cooking methods, diet) differ greatly between Asian and Western populations. The potential effects of such factors must be considered when evaluating the results of epidemiologic studies on lung cancer incidence, particularly those considering ETS exposure. Table 1 presents a comparison and summary of Asian studies to date, revealing the increasing attention paid to confounders in these studies.

Dr. Linda Koo, in her 1988 paper on lifestyle correlates, summed up the importance of confounders as follows:

> [C]aution should be exercised when interpreting data on ETS. It may not be the hazards of tobacco smoke that are being evaluated, but a whole range of behaviors that result from having a smoking husband, which may in turn increase the risk for certain diseases among their wives and children.[16]

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Table 1a. Asian Studies Included in EPA Draft Risk Assessment: Epidemiologic Studies of Lung Cancer in Nonsmoking Women, with Spousal Smoking Included

Study [site]	Sample Size	Spousal Smoking*	Factors Considered: Heating Methods/ Fuel Use	Cooking Tech-Niques	Diet	Other
Hirayama, 1981, 1984 [Japan]	91,540	(+)	--	--	--	--
Chan and Fung, 1982 [Hong Kong]	223	(-)	--	Yes	--	--
Lam, 1985 [Hong Kong]	248	(-)	--	Yes	--	Home incense burning
Akiba, et al., 1986 [Japan]	1,385	(+)	--	--	--	Radiation exposure
Gao, et al., 1987 [Shanghai]	1,407	(-)	--	Yes	Yes	Medical history; hormonal factors
Koo, et al., 1987 [Hong Kong]	225	(-)	--	--	--	--
Lam, et al., 1987 [Hong Kong]	890	(+)	--	--	--	--
Geng, et al., 1988 [Tianjin, China]	314	(+)	Yes	--	--	Medical history; occupation
Inoue and Hirayama, 1988 [Japan]	83	(+)	--	--	--	--

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Study [site]	Sample Size	Spousal Smoking*	Factors Considered: Heating Methods/ Fuel Use	Cooking Tech-Niques	Diet	Other
Shimizu, et al., 1988 [Japan]	180	(-)	Yes	--	Yes	Occupation

* (+) indicates a statistically significant relative risk was reported; (-) indicates the reported relative risk was not statistically significant.

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Table 1b. Asian Studies Published After EPA Draft Risk Assessment: Epidemiologic Studies of Lung Cancer in Nonsmoking Women, with Spousal Smoking Included

Study [site]	Sample Size	Spousal Smoking*	Factors Considered: Heating Methods/ Fuel Use	Cooking Tech-Niques	Diet	Other
He, et al., 1990 [China]	536+	(-)	Yes	Yes	--	Medical history
Sobue, et al., 1990 [Japan]	639	(-)	Yes	--	--	--
Wang, et al., 1990 [NE China]	110	(-)	Yes	--	--	Indoor and outdoor air pollution
Wu-Williams, et al., 1990 [NE China]	1,924	(+)**	Yes	Yes	Yes	Medical history; occupation
Liu, et al., 1991*** [China]	221	(-)	Yes	Yes	--	Medical history

* (+) indicates a statistically significant relative risk was reported; (-) indicates the reported risk was not statistically significant.
\+ Males and females combined.
** The reported relative risk was statistically significantly negative.
***Full report on population discussed in He, et al., abstract.

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Table 1c. Ancillary Asian Studies, Not Considered in EPA Draft Risk Assessment

Study [site]	Sample Size	Factors Considered: Spousal Smoking	Heating Methods/ Fuel Use	Cooking Tech-Niques	Diet	Other
Koo, et al., 1984 [Hong Kong]	400	No**	--	--	--	--
Mumford, et al., 1987 [China]	--	No	Yes	--	--	--
Chapman, et al., 1988 [China]	144+	No	Yes	--	--	--
Koo, et al., 1988 [Hong Kong]	136	No	--	--	Yes	Lifestyle variables
Du and Ou, 1990 [China]	1,324	No	Yes	--	--	--
Xu, et al., 1990 [NE China]	1,077	No	Yes	Yes	Yes	Indoor and outdoor air pollution; occupation

** Other questions were asked regarding ETS.
+ Males and females combined.

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A selection of the relevant literature follows. Useful information is highlighted in yellow; problematic statements are highlighted in blue.

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